SHORT PAPER

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Synthesis of four novel benzimidazole derivatives mediated by manganous acetate – permanganate mixture[†]

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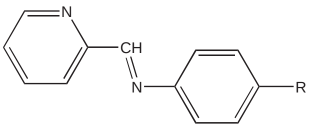
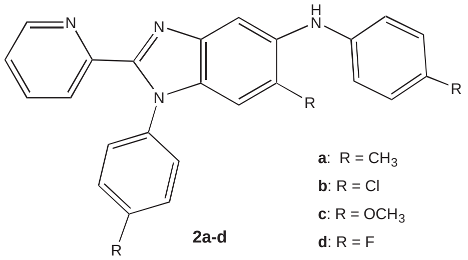
The synthesis is described of four novel benzimidazole derivatives from substituted *N*-phenyl pyridine-2-aldimine Schiff bases mediated by manganous acetate – potassium permanganate mixture.

Keywords: benzimidazoles, aldimines, pyridines, manganese(II/VII), crystal structure, radical reactions

Formation of carbon–carbon and carbon–oxygen bonds mediated by transition metal complexes is now a well studied field.[1,2] However, efficient methods for carbon–nitrogen bond formation (except the N-alkylation / arylation of azoles), possibly through the intermediacy of transition metal complexes, is a less developed, though much sought-after, process.[2] This is because of the importance of organo-nitrogen compounds in biological and medicinal chemistry. One such important class of compounds is imidazole and its derivatives. In this paper we describe a manganous acetate – permanganate mediated C-N bond formation in the synthesis of four novel benzimidazole derivatives (**2a–d**) starting from simple Schiff bases (**1a–d**).



1a-d



2a-d

Results and discussion

The compounds **2a–d** were obtained by reacting the Schiff bases **1a–d** (3 mmole) with manganous acetate (1 mmole) and potassium permanganate (0.65 mmole) under ice-cold conditions followed by acidification with aqueous $HClO_4$ (35%). Recrystallisation of the crude product from acetonitrile – diethyl ether afforded greenish-brown X-ray quality crystals. The structure of the perchlorate salt of **2a** was determined by X-ray crystallography. An ORTEP diagram including the atom numbering scheme is shown in Fig. 1. Table 1 gives some selected bond distances and bond angles. All the C–N bond distances within the imidazole ring as well as the C(17)–N(4) distance lies in between the normal carbon-nitrogen single bond (1.47 Å) and double bond (1.32 Å) distances.[3] The C(5)–C(6) bond (1.481 Å) connecting the pyridine and imidazole rings is also considerably shorter than a normal single bond (1.54 Å) distance.[3] The bond distances clearly indicate that there is considerable delocalistion between the pyridine and imidazole rings. The C(7)–N(2) and C(21)–N(4) bond distances are however close to a normal C–N single bond distance.

Table 1 Some important bond lengths (Å) and angles (°) in **2a**

Bond	Distance	Bond	Distance	Bonds	Angle
C1–N1	1.341(4)	C6–N3	1.338(4)	C5–C6–N3	124.3(3)
C5–N1	1.339(4)	C15–N3	1.390(4)	C5–C6–N2	126.3(3)
C6–N2	1.324(4)	C17–N4	1.391(4)	C7–N2–C14	123.2(3)
C7–N2	1.446(4)	C21–N4	1.406(4)	C7–N2–C6	127.5(3)
C4–N2	1.409(4)	C5–C6	1.481(4)	C17–N4–C21	127.6(3)
		C14–C15	1.373(4)		

Mn(III) compounds, particularly 'Mn(OAc)$_3$', Mn(porph)X (porph = porphyrin and its derivatives) are known to be efficient reactants / catalysts for a variety of reactions that form C–C and C–O bonds.[4-8] There are also some relatively rare examplesof Mn(III) mediated C–N bond forming reactions.[9,10] In the present study, a Mn(IV) compound could be contemplated, based on the stoichiometry of the reaction, as the active species in the organic

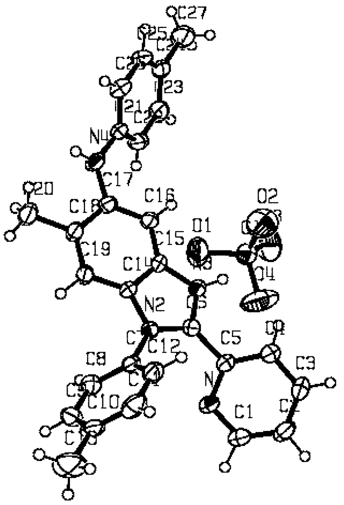


Fig.1 ORTEP diagram of **2a**.$HClO_4$.

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[†] This is a Short Paper, there is therefore no corresponding material in *J Chem. Research (M).*

transformation. However, Mn(IV) mediated C–N bond formation is unknown, and Mn(IV) compounds, being d^3 species, are substitutionally inert and therefore unlikely to participate in any substrate interactions. It is likely therefore that a Mn(III) species is involved in this process as well. The stoichiometric excess of MnO_4^- remaining after formation of the initial Mn(III) species may be utilised to regenerate Mn(III) after its reaction with the organic substrate.[11]

The formation of **2** from **1** in a single-pot one-step synthesis is an interesting reaction. Benzimidazoles are normally prepared by reacting 1,2-diaminobenzene with carboxylic acids or their derivatives, or with carbaldehydes in oxidative environment. To our knowledge this is the first reported synthesis of a series of benzimidazoles starting from an imine. The reaction mechanism is probably similar to the phenolic coupling reaction in which a phenoxide ion is oxidized to a phenoxy radical, stabilised by delocalization involving the phenyl group. Two phenoxy radicals then dimerize with formation of a new carbon–carbon bond. In the present case, the reaction is probably initiated by hydrolysis of the Schiff base to form the free amine. Inasmuch as most of the Mn(III) mediated organic transformations for which the mechanisms are known[7] proceed by radical mechanisms, it is possible the amine is converted into PhNH·, which then reacts with another molecule of the Schiff base **1** in the presence of Mn(III) to form the benzimidazole ring. The phenyl ring of the benzimidazole is then aminated[12] at the 5-position by a second PhNH·radical.

The proposed formation of PhNH·is supported by the isolation of appropriately substituted azobenzenes (PhN=NPh) from the reaction medium. Interestingly, recently Matsushita *et al.*[13] reported the formation of benzoxazole derivatives in the reaction of $KMnO_4$ with *N*-(2-hydroxyphenyl)salicylideneamine, and the reaction was shown to proceed through a radical mechanism, similar to that we have proposed here.

Experimental

Synthesis of **2a**.*$HClO_4$*: To a methanolic solution (20 ml) of the Schiff base **1a** (3 mmol, 588 mg), an aqueous solution (10 ml) of $Mn(OAc)_2$.$4H_2O$ (1 mmol, 246 mg) was added with stirring, followed by glacial acetic acid (2 ml). The solution was then cooled in an ice bath and an aqueous solution (10 ml) of $KMnO_4$ (0.65 mmol, 70 mg) was added drop by drop. After 30 min, the solution was filtered and to the filtrate aqueous perchloric acid (2 ml, 35%) was added dropwise. After two hours the solution was filtered, the residue washed with water and dried over fused calcium chloride. The solid was then dissolved in acetonitrile and recrystallised by diffusion of diethyl ether into the acetonitrile solution (yield ~20%).

2b.*$2HClO_4$.1.5MeOH* (yield 23%), **2c.**$2HClO_4$ (yield 20%). and **2d**.$HClO_4$ (yield 22%) were isolated by a similar procedure from **1b, 1c** and **1d** respectively. All the products were satisfactorily characterised by C, H, N analysis and FAB mass spectrometry.

Analytical data: (**2a**.$HClO_4$, found: C, 64.3; H, 5.0; N, 11.2; calc. for $C_{27}H_{25}ClN_4O_4$ C, 64.2; H, 4.9; N, 11.1. FAB MS: *m/z* 405 $[MH]^+$, 314 $[MH – C_7H_7]^+$.

2b.*$2HClO_4$.1.5 MeOH*, C, 42.8; H, 3.4; N, 8.0; calc. for $C_{25.5}H_{23}Cl_5N_4O_{9.5}$ C, 42.8; H, 3.2; N, 7.8; FAB MS: *m/z*:354 $[MH – C_6H_4Cl]^+$, 243 $[MH – 2C_6H_4Cl]^+$, 228 $[MH – C_6H_4Cl – HNC_6H_4Cl]^+$.

2c.*$2HClO_4$*: found C, 49.9; H, 3.9; N, 8.6; calc. for $C_{27}H_{26}Cl_2N_4O_{11}$ C, 49.6; H, 4.0; N, 8.6; FAB MS: *m/z* 453 $[MH]^+$, 346$[MH – C_7H_7O]^+$.

2d.*$HClO_4$*, C, 55.8; H, 3.2; N, 10.7; calc. for $C_{24}H_{16}ClF_3N_4O_4$ C, 55.7; H, 3.0; N, 10.8; FAB MS: *m/z* 307 $[MH^+ – NHC_6H_4F]^+$, 289 $[MH^+–NHC_6H_4F – F + H]^+$.

Crystal data: $C_{27}H_{25}O_4N_4Cl$, M= 504.92, triclinic (primitive), a = 10.366(1), b = 14.315(2), c = 9.363(1)Å, V= 1217.2(3)$Å^3$, space group P1(No.2) , Z= 2, $\mu(Mo\text{-}K_\alpha)$ = 1.99 cm^{-1}, 5940 reflections measured, 5629 unique (R_{int} = 0.021) , 3428 observed reflections ($I > 2.0\ \sigma(I)$) , R = 0.058, R_w = 0.060, GOF =2.23

The structure was solved by direct methods (SIR92)[13]. The non-hydrogen atoms were refined anisotropically. Neutral atom scattering factors and anomalous dispersion effects were included. Further details of the crystal structure analysis may be obtained from the Author.

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References

1 F.A. Cotton, G. Wilkinson, C.A. Murillo, and M. Bochmann, *Advanced Inorganic Chemistry*, 6th edn, Wiley, New York, 1999, Ch. 22.
2 J.F. Hartwig, *Angew. Chem. Int. Ed. Eng.*, 1998, **37**, 2046.
3 J.L. Huheey, E.A. Keiter, and R.L. Leiter, *Inorganic Chemistry*, 4th edn, Harper Collins, 1993, A30.
4 B.B. Snider, *Chem. Rev.*, 1996, **96**, 339.
5 G.G. Melikyan, *Synthesis*, 1993, 833.
6 G.G. Melikyan, in *Organic Reactions,* Vol. 49: Paquette L. A. Ed., J. Wiley, New York, NY, (1997), pp. 427-675.
7 E.I. Heiba, R.M. Dessau, and W.E. Koehl, *J. Am. Chem. Soc.*, 1969, **91**, 131.
8 (a) P.J. Andrulis jr, M.J.S. Dewar, R. Deitz, and R.I. Hunt, *J. Am. Chem. Soc.*,1966, **88**, 5473; (b) T. Arantani and M.J.S. Dewar, *J. Am. Chem. Soc.*, 1966, **88**, 5429.
9 A. Evans, M.M. Faul, and M.T. Bilodeau, *J. Am. Chem. Soc.*, 1994, **116**, 2742.
10 J. Yang, R. Weinberg, and R. Breslow, *Chem. Commun.*, 2000, 531.
11 U. Linker, B. Kersten, and T. Linker, *Tetrahedron*, 1995, **51**, 9917.
12 V.G.S. Box and H.W. Yu , *J. Chem. Edu.*, 1997, **74**, 1293.
13 H. Asada, M. Ozeki, M. Fujiwara, and T. Matsushita, *Polyhedron*, 2002, **21**, 1139.
14 SIR92: A. Altomare, M. Cascarano, C. Giacovazzo, and A. Guagliardi, *J. Appl. Cryst.*, 1993, **26**, 343.